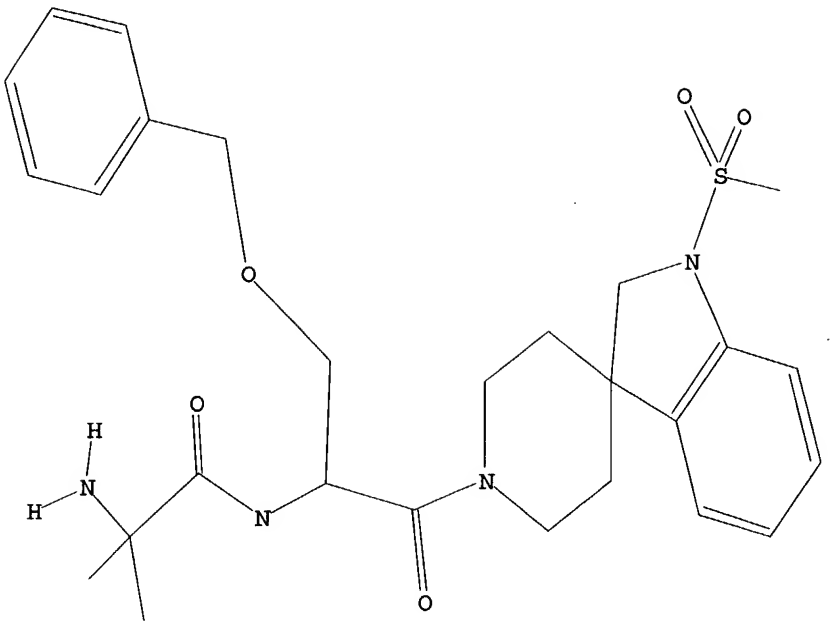
5/13/2004

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 304853-26-7 REGISTRY
CN Ghrelin (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Growth hormone secretagogue



Structure attributes must be viewed using STN Express query preparation.

```
=> s l1
SAMPLE SEARCH INITIATED 14:54:50 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     14 TO ITERATE

100.0% PROCESSED      14 ITERATIONS                                4 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:           56 TO      504
PROJECTED ANSWERS:               4 TO      200

L2            4 SEA SSS SAM L1

=> s l1 ful
FULL SEARCH INITIATED 14:54:54 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    204 TO ITERATE

100.0% PROCESSED     204 ITERATIONS                              37 ANSWERS
SEARCH TIME: 00.00.01

L3           37 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             155.42     155.63
```

5/13/2004

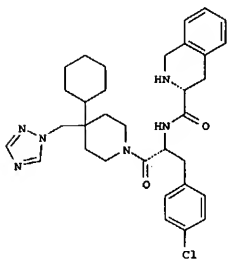
FILE 'CAPLUS' ENTERED AT 14:54:59 ON 19 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 19 May 2004 VOL 140 ISS 21
FILE LAST UPDATED: 18 May 2004 (20040518/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s l3
L4          105 L3

=> s l3 and (food or diabetes or anorexia or  or lack of appetite)
MISSING TERM 'OR  OR'
The search profile that was entered contains a logical
operator followed immediately by another operator.

=> s l3 and (food or diabetes or anorexia or lack of appetite)
            105 L3
         291349 FOOD
          66103 FOODS
         310265 FOOD
                   (FOOD OR FOODS)
          88894 DIABETES
           5286 ANOREXIA
              7 ANOREXIAS
           5286 ANOREXIA
                   (ANOREXIA OR ANOREXIAS)
         136367 LACK
          18410 LACKS
         153525 LACK
                   (LACK OR LACKS)
          20366 APPETITE
            170 APPETITES
          20450 APPETITE
                   (APPETITE OR APPETITES)
             60 LACK OF APPETITE
                   (LACK(1W)APPETITE)
L5            6 L3 AND (FOOD OR DIABETES OR ANOREXIA OR LACK OF APPETITE)

=> d abs bib hitstr 1-6
```

L5 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
GI

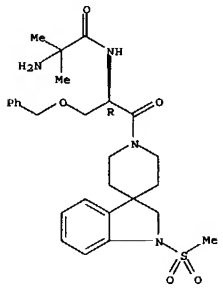


I

AB Synthetic and natural peptides that act as nonselective melanocortin receptor agonists have been found to be anorexigenic and to stimulate erectile activity. We report the design and development of (I), a potent, selective (1184-fold vs. MC3R, 350-fold vs. MC5R), small-mol. agonist of the MC4 receptor. Pharmacol. testing confirms the food intake lowering effects of MC4R agonism and suggests another role for the receptor in the stimulation of erectile activity.
AN 2002:699493 CAPLUS
DN 137:362928
TI Design and pharmacology of N-[(3R)-1,2,3,4-tetrahydroisoquinolinium-3-ylcarbonyl]-(1R)-1-(4-chlorobenzyl)-2-[4-cyclohexyl-4-(1H-1,2,4-triazol-1-ylmethyl)piperidin-1-yl]-2-oxoethylamine (1), a potent, selective, melanocortin subtype-4 receptor agonist
AU Sebhat, Iyassu K.; Martin, William J.; Ye, Zhixiong; Barakat, Khaled; Mosley, Ralph T.; Johnston, David B. R.; Bakshi, Raman; Palucki, Brenda; Weinberg, David H.; MacNeil, Tanya; Kalyani, Rubana N.; Tang, Rui; Stearns, Ralph A.; Miller, Randy R.; Tamvakopoulos, Constantin; Strack, Alison M.; McGowan, Erin; Cashen, Doreen E.; Driskо, Jennifer E.; Hom, Gary J.; Howard, Andrew D.; MacIntyre, D. Euan; van der Ploeg, Lex H. T.; Patchett, Arthur A.; Nargund, Ravi P.
CS Departments of Chemistry, Pharmacology, Obesity Research, and Drug Metabolism, Merck Co. Inc., Rahway, NJ, 07065-0900, USA
SO Journal of Medicinal Chemistry (2002), 45(21), 4589-4593
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English

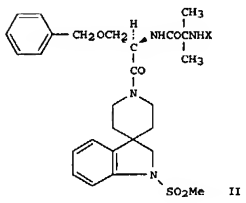
L5 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
IT **159634-47-6**
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(design and pharmacol. of melanocortin 4 receptor agonist)
RN 159634-47-6 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
GI



II

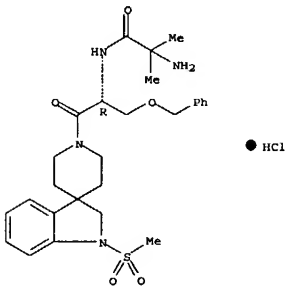
AB This invention is concerned with polymorphic forms of the compound N-[1(R)-[(1,2-dihydro-1-methanesulfonylspiro[3H-indole-3,4'-piperdin]-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide methanesulfonate (I). I is a growth hormone secretagogue that is useful in food animals to promote their growth thereby rendering the production of edible meat products more efficient, and in humans, to treat physiol. or medical conditions. The present invention is also concerned with the formulations in the treatment of certain disorders. Thus, compound (II; X = BOC) (preparation given) was treated with MeSO3H to give the title compound II.MeSO3H (X = H).
AN 1998:414732 CAPLUS
DN 129:67698
TI Polymorphic forms of a growth hormone secretagogue
IN Draper, Jerome P.; Kaufman, Michael J.; Dubost, David C.; McCauley, James A.; Vandrilla, Jennifer L.; Varsolona, Richard J.
PA Merck and Co., Inc., USA
SO U.S., 25 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5767124	A	19980616	US 1996-736170	19961023
CN 1205703	A	19990120	CN 1996-199328	19961023
CN 1067687	B	20010627		
PRAI US 1996-736170	A	19961023		

OS CASREACT 129:67698
IT **159633-92-8P 159634-47-6P 159752-10-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminomethylpropanamide derivs. for the treatment of physiol. or medical conditions and certain disorders)
RN 159633-92-8 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-

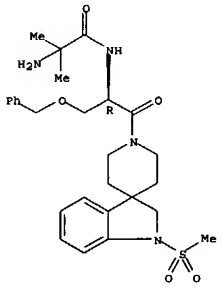
L5 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 159634-47-6 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



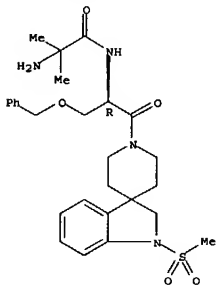
RN 159752-10-0 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-

L5 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
methyl-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 159634-47-6
CMF C27 H36 N4 O5 S

Absolute stereochemistry.

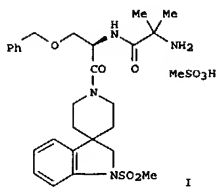


CM 2

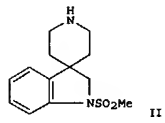
CRN 75-75-2
CMF C H4 O3 S

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
GI



I



II

AB A novel convergent process for the preparation of the compound
N-[1(R)-[(1,2-dihydro-1-methanesulfonyl-spiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide methanesulfonamide (I) is claimed. The above compound I is synthesized from the reactants (R)-PhCH2OCH2CH(NH2)CO2Me, BocNHC(Me2)CO2H and spiro compound II (which is synthesized in several steps from isonipecotic acid, PhNHNH2 and MeSO2Cl) with an overall yield of 56% and 99.9% purity. This compound may be used to treat conditions which require the stimulation of growth hormone production, or secretion such as in humans with a deficiency of natural growth hormone, or in animals used for food or wool production where the stimulation of growth hormone will result in a larger, more productive animal.
AN 1998:293521 CAPLUS
DN 128:321949
TI Preparation of N-[1(R)-[(1,2-dihydro-1-methanesulfonyl-spiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide methanesulfonamide, a growth hormone secretagogue
IN Dorziotis, Ilias; Houpis, Ioannis; Molina, Audrey; Volante, Ralph
PA Merck & Co., Inc., USA; Dorziotis, Ilias; Houpis, Ioannis; Molina, Audrey; Volante, Ralph
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9818815	A1	19980507	WO 1997-US19063	19971021

L5 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

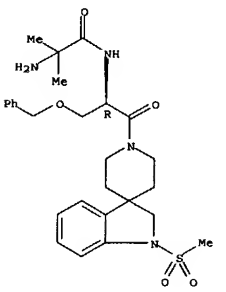
	AU 9749934	A1	19980522	AU 1997-49934	19971021
	US 6046333	A	20000404	US 1997-955124	19971021
PRAI	US 1996-29454P	P	19961025		
	GB 1996-25815	A	19961212		
	WO 1997-US19063	W	19971021		

IT **159752-10-0P**
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation of spiroindolepiperidinyl derivative of aminoisobutyrylserinamide as a growth hormone secretagogue)
RN 159752-10-0 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 159634-47-6
CMF C27 H36 N4 O5 S

Absolute stereochemistry.



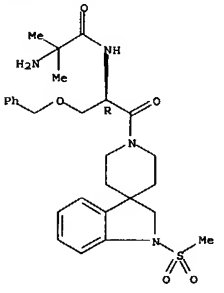
CM 2

CRN 75-75-2
CMF C H4 O3 S

L5 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

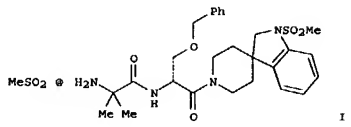
IT **159634-47-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of spiroindolepiperidinyl derivative of aminoisobutyrylserinamide as a growth hormone secretagogue)
RN 159634-47-6 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

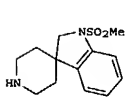


RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

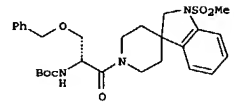
L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
GI



I



II

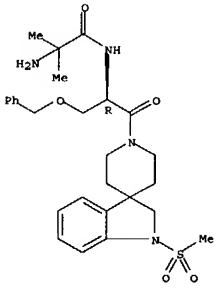


III

AB The present invention is directed to a novel process for the preparation of N-[1(R)-[(1,2-dihydro-1-methanesulfonylspiro[3H-indole-3,4'-piperdin]-1'-yl)carbonyl]-2-(benzyloxy)ethyl]-2-amino-2-methylpropanamide methanesulfonate (I) and which has the ability to stimulate the release of natural or endogenous growth hormone. I may be used to treat conditions which require the stimulation of growth hormone production or secretion such as in humans with a deficiency of natural growth hormone or in animals used for food or wool production where the stimulation of growth hormone will result in a larger, more productive animal. Thus, peptide coupling of spiropiperidine II (preparation given) with Boc-D-Ser(CH2Ph)-OH (Boc = Me3CO2C) in the presence of DCC and HOBt in aqueous iso-Pr acetate gave 93% adduct III, which was deprotected with MeSO3H in MeOH or EtOH, further coupled with Boc-Aib-OH (Aib = α-aminoisobutyric acid) using DCC and HOBt in aqueous iso-Pr acetate, deprotected with MeSO3H in EtOH, and converted into salt I with MeSO3H in EtOAc.

AN 1998:165466 CAPLUS
DN 128:205149
TI Process for the preparation of a growth hormone secretagogue
IN Houghton, Peter G.; Molina, Audrey; Houpis, Joannis; Lynch, Joseph E.; Volante, Ralph P.
PA Merck and Co., Inc., USA
SO U.S., 24 pp.
CODEN: USXXAM

L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **159752-10-0P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparation of growth hormone secretagogue using DCC in aqueous iso-Pr acetate)
RN 159752-10-0 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 159634-47-6
CMF C27 H36 N4 O5 S

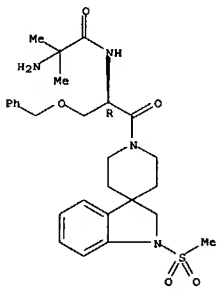
Absolute stereochemistry.

L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5723616	A	19980303	US 1996-736173	19961023
PRAI	US 1996-736173		19961023		

OS CASREACT 128:205149
IT **159634-47-6DP**, N-protected deriva. **159634-47-6P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of growth hormone secretagogue using DCC in aqueous iso-Pr acetate)
RN 159634-47-6 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)

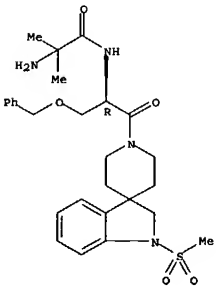
Absolute stereochemistry.



RN 159634-47-6 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



CM 2

CRN 75-75-2
CMF C H4 O3 S

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

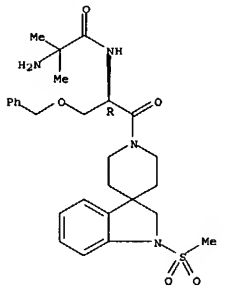
AB A review with 183 refs. Growth hormone-releasing peptides (GHRPs) are synthetic, non-natural peptides endowed with potent stimulatory effects on somatotrope secretion in animals and humans. They have no structural homol. with GHRH and act via specific receptors present either at the pituitary or the hypothalamic level both in animals and in humans. The GHRP receptor has been cloned and, interestingly, it does not show sequence homol. with other G-protein-coupled receptors known so far. This evidence strongly suggests the existence of a natural GHRP-like ligand which, however, has not yet been found. The mechanisms underlying the GHRP effect are still unclear. At present, several data favor the hypothesis that GHRPs could act by counteracting somatostatinergic activity both at the pituitary and the hypothalamic level and/or, at least partially, via a GHRH-mediated mechanism. However, the possibility that GHRPs act via an unknown hypothalamic factor (U factor) is still open. GHRP-6 was the first hexapeptide to be extensively studied in humans. More recently, a heptapeptide, GHRP-1, and two other hexapeptides, GHRP-2 and Hexarelin, have been synthesized and are now available for human studies. Moreover, non-peptidyl GHRP mimetics have been developed which act via GHRP receptors and their effects have been clearly demonstrated in animals and in humans in vivo. Among non-peptidyl GHRPs. MK-0677 seems the most interesting mol. The GH-releasing activity of GHRPs is marked and dose-related after i.v., s.c., intranasal and even oral administration. The effect of GHRPs is reproducible and undergoes partial desensitization, more during continuous infusion, less during intermittent administration: in fact, prolonged administration of GHRPs increases IGF-I levels both in animals and in humans. The GH-releasing effect of GHRPs does not depend on sex but undergoes age-related variations. It increases from birth to puberty, persists at a similar level in adulthood and decreases thereafter. By the sixth decade of life, the activity of GHRPs is reduced but it is still marked and higher than that of GHRH. The GH-releasing activity of GHRPs is synergistic with that of GHRH, is not affected by opioid receptor antagonists, such as naloxone, and is only blunted by inhibitory influences, including neurotransmitters, glucose, free fatty acids, glucocorticoids, recombinant human GH and even exogenous somatostatin, which are known to almost abolish the effect of GHRH. GHRPs maintain their GH-releasing effect in somatotrope hypersecretory states such as in acromegaly, **anorexia** nervosa and hyperthyroidism. Their good GH-releasing activity has been shown in some but not in other somatotrope hyposecretory states. In fact, reduced GH responses after GHRP administration have been reported in idiopathic GH deficiency as well as in idiopathic short stature, in obesity and in hypothyroidism, while in patients with pituitary stalk disconnection or Cushing's syndrome the somatotrope responsiveness to GHRPs is almost absent. In short children an increase in height velocity has also been reported during chronic GHRP treatment. Thus, based on their marked GH-releasing effect even after oral administration, GHRPs offer their own clin. usefulness for treatment of some GH hyposecretory states.

AN 1997:375774 CAPLUS
DN 127:90522
TI Growth hormone-releasing peptides
AU Ghigo, E.; Arvat, E.; Muccioli, G.; Camanni, F.
CS Division of Endocrinology, Dep. of Internal Medicine and Division of Pharmacology, Dep. of Anatomy, Pharmacology and Forensic Medicine, University of Turin, Italy
SO European Journal of Endocrinology (1997), 136(5), 445-460
CODEN: EJOEEP; ISSN: 0804-4643
PB BioScientifica
DT Journal; General Review
LA English
IT **159752-10-0**, MK 677
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(growth hormone-releasing peptides)
RN 159752-10-0 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 159634-47-6
CMF C27 H36 N4 O5 S

Absolute stereochemistry.



L5 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

CM 2

CRN 75-75-2
CMF C H4 O3 S

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB There are disclosed certain novel compds. identified as spiro piperidines and homologs I and II wherein: R1 = e.g., C1-10 alkyl, aryl, aryl-(C1-6 alkyl); R2 = e.g., H, C1-6 alkyl, C3-7 cycloalkyl; R3a and R3b are independently, e.g., H, halo, C1-6 alkyl; R4 and R5 are independently, H, C1-6 alkyl, substituted C1-6 alkyl where the substituents on alkyl are, e.g., 1 to 5 halo, 1 to 3 hydroxy; R6 is H or C1-6 alkyl; A is (CH2)xCR7R7a(CH2)y or Z(CH2)xCR7R7a(CH2)y wherein x and y are independently 0, 1, 2, or 3; Z is NR2 or O; R7 and R7a are independently, e.g., H, C1-6 alkyl, OR2; B, D, E, and F are independently selected from CR8R10, O, CO, SOm, NR9, wherein one or two of B, D, E, or F may be optionally absent to provide a 5, 6, or 7-membered ring; R8 and R10 are independently, e.g., H, R2, OR2; R9 = e.g., R2, COR2, SO2R2; m is 0, 1, or 2; n is 1 or 2; G, H, I and J are carbon, nitrogen, sulfur or oxygen atoms, such that one or two is a heteroatom, and where one of G, H, I or J may be optionally absent to afford a 5 or 6 membered heterocyclic aromatic ring; and the pharmaceutically acceptable salts and individual diastereomers thereof, which promote the release of growth hormone in humans and animals (no data). This property can be utilized to promote the growth of **food** animals to render the production of edible meat products more efficient, and in humans, to treat physiol. or medical conditions characterized by a deficiency in growth hormone secretion, such as short stature in growth hormone deficient children, and to treat medical conditions which are improved by the anabolic effects of growth hormone. Growth hormone releasing compns. containing such spiro compds. as the active ingredient thereof are also disclosed. Thus, e.g., 1'-(t-butyloxycarbonyl)spiro[1H-indene-1,4'-piperidine] was subjected to hydroboration/oxidation, to provide 1'-(t-butyloxycarbonyl)-2,3-dihydro-3-oxospiro[1H-indene-1,4'-piperidine]; deprotection followed by trifluoroacetylation afforded the trifluoroacetamide; Schmidt reaction of the latter provided 3,4-dihydro-2-oxospiro[piperidine-4,4'(1H)-quinoline] trifluoroacetamide (together with its spiroisoquinoline isomer); saponification followed by coupling with α(R)-[[2-[[(1,1-dimethylethoxy)carbonyl]amino]-2,2-dimethyl-1-oxoethyl]amino]-1H-indole-3-propanoic acid (preparation given) and deprotection provided N-[1(R)-[(3,4-dihydro-2-oxospiro[piperidine-4,4'(1H)-quinolin]-1'-yl)carbonyl]-2-(indol-3-yl)ethyl]-2-amino-2-methylpropanamide hydrochloride (III.HCl).

AN 1996:469925 CAPLUS
DN 125:196372
TI Spiro piperidines which promote release of growth hormone
IN Chen, Meng-Hsin; Johnston, David B. R.; Nargund, Ravi P.; Patchett, Arthur A.; Tata, James R.; Yang, Lihu
PA Merck and Co., Inc., USA

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
SO U.S., 48 pp., Cont.-in-part of U.S. Ser. No. 989, 322, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

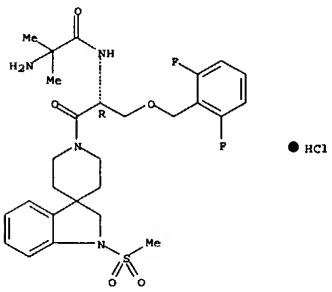
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5536716	A	19960716	US 1993-147226	19931103
	WO 9413696	A1	19940623	WO 1993-US11038	19931115
	W: BB, BG, BR, BY, CZ, FI, HU, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ				
	RW: BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	WO 9419367	A1	19940901	WO 1993-US11137	19931115
	W: BB, BG, BR, BY, CZ, FI, HU, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ				
	RW: BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	HU 72076	A2	19960328	HU 1995-1683	19931115
	HU 73228	A2	19960729	HU 1995-1681	19931115
	PL 176993	B1	19990831	PL 1993-309331	19931115
	RU 2168512	C2	20010610	RU 1995-113349	19931115
	SK 282166	B6	20011106	SK 1995-759	19931115
	CA 2110670	AA	19940612	CA 1993-2110670	19931203
	CA 2110670	C	20010417		
	CA 2110672	AA	19940612	CA 1993-2110672	19931203
	EP 615977	A1	19940921	EP 1993-309867	19931208
	EP 615977	B1	20020703		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	AT 220071	E	20020715	AT 1993-309867	19931208
	PT 615977	T	20021031	PT 1993-309867	19931208
	ES 2177538	T3	20021216	ES 1993-309867	19931208
	AU 9352320	A1	19940623	AU 1993-52320	19931210
	AU 672552	B2	19961114		
	AU 9352321	A1	19940623	AU 1993-52321	19931210
	AU 673017	B2	19961024		
	ZA 9309272	A	19940808	ZA 1993-9272	19931210
	ZA 9309274	A	19940808	ZA 1993-9274	19931210
	JP 06263737	A2	19940920	JP 1993-341522	19931210
	JP 2509530	B2	19960619		
	HR 931486	B1	20030831	HR 1993-931486	19931210
	CN 1092071	A	19940914	CN 1993-112858	19931211
	CN 1034733	B	19970430		
	FI 9502862	A	19950609	FI 1995-2862	19950609
	FI 9502863	A	19950609	FI 1995-2863	19950609
	NO 9502294	A	19950810	NO 1995-2294	19950609
	NO 9502295	A	19950810	NO 1995-2295	19950609
	US 5652235	A	19970729	US 1996-641311	19960430
PRAI	US 1992-989322	B2	19921211		
	US 1993-146848		19931103		
	US 1993-147226	A	19931103		
	WO 1993-US11038	W	19931115		
	WO 1993-US11137	W	19931115		

OS MARPAT 125:196372
IT **159633-90-6P 159633-92-8P 159633-94-0P**
159634-09-0P 159634-10-3P 159634-12-5P
159634-13-6P 159634-37-4P 159634-47-6P

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
159634-49-8P 159634-50-1P 159752-10-0P
180465-75-2P 180465-79-6P 180465-80-9P
180466-14-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(spiro piperidines which promote release of growth hormone)

RN 159633-90-6 CAPLUS
CN Propanamide, 2-amino-N-[1-[[(2,6-difluorophenyl)methoxy]methyl]-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxoethyl]-2-methyl-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

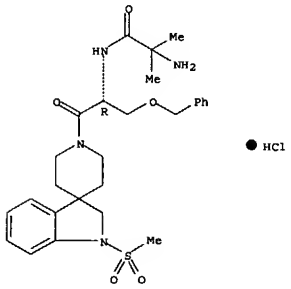
Absolute stereochemistry.



RN 159633-92-8 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

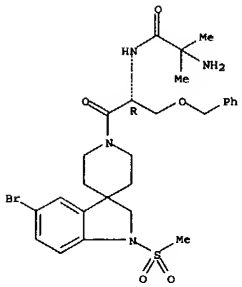


RN 159633-94-0 CAPLUS
CN Propanamide, 2-amino-N-[2-[5-bromo-1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, (R)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 159633-93-9
CMF C27 H35 Br N4 O5 S

Absolute stereochemistry.

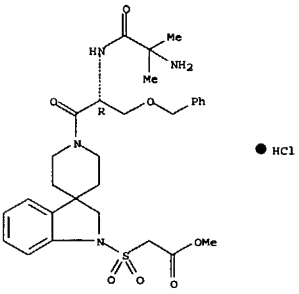


L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 159634-09-0 CAPLUS
CN Acetic acid, [[1'-[2-[(2-amino-2-methyl-1-oxopropyl)amino]-1-oxo-3-(phenylmethoxy)propyl]spiro[3H-indole-3,4'-piperidin]-1(2H)-yl]sulfonyl]-, methyl ester, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

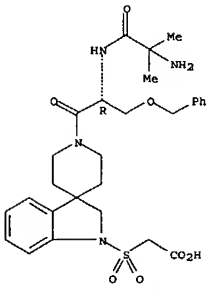
Absolute stereochemistry.



RN 159634-10-3 CAPLUS
CN Acetic acid, [[1'-[2-[(2-amino-2-methyl-1-oxopropyl)amino]-1-oxo-3-(phenylmethoxy)propyl]spiro[3H-indole-3,4'-piperidin]-1(2H)-yl]sulfonyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



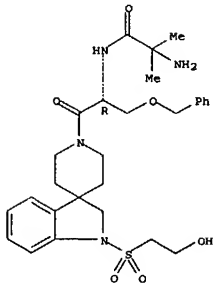
RN 159634-12-5 CAPLUS
CN Propanamide, 2-amino-N-[2-[1,2-dihydro-1-[(2-hydroxyethyl)sulfonyl]spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, (R)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 159634-11-4
CMF C28 H38 N4 O6 S

Absolute stereochemistry.

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



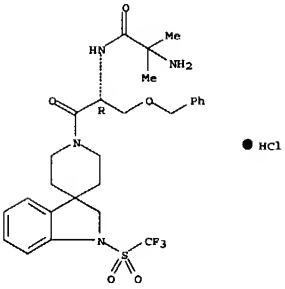
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 159634-13-6 CAPLUS
CN Propanamide, 2-amino-N-[2-[1,2-dihydro-1-[(trifluoromethyl)sulfonyl]spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

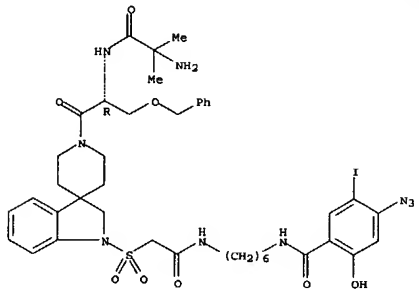


● HCl

RN 159634-37-4 CAPLUS
CN Benzamide, N-[6-[[[[1'-[2-[(2-amino-2-methyl-1-oxopropyl)amino]-1-oxo-3-(phenylmethoxy)propyl]spiro[3H-indole-3,4'-piperidin]-1(2H)-yl]sulfonyl]acetyl]amino]hexyl]-4-azido-2-hydroxy-5-iodo-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



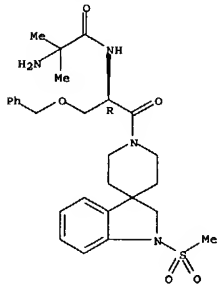
L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A

● HCl

RN 159634-47-6 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)

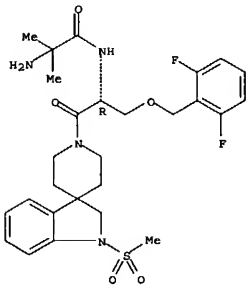
Absolute stereochemistry.



RN 159634-49-8 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-1-[[(2,6-difluorophenyl)methoxy]methyl]-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxoethyl]-2-methyl- (9CI) (CA INDEX NAME)

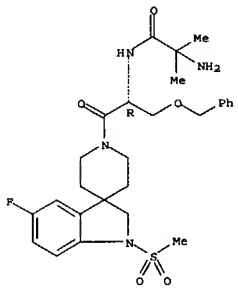
Absolute stereochemistry.

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



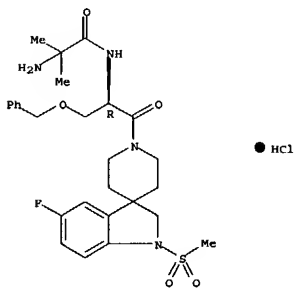
RN 159634-50-1 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[5-fluoro-1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



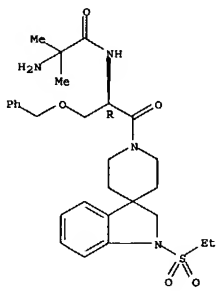
RN 159752-10-0 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 180465-79-6 CAPLUS
CN Propanamide, 2-amino-N-[2-[1-(ethylsulfonyl)-1,2-dihydrospiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 180465-80-9 CAPLUS
CN Propanamide,
2-amino-N-[2-[1,2-dihydro-1-[(1-methylethyl)sulfonyl]spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, (R)- (9CI) (CA INDEX NAME)

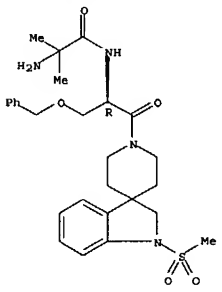
Absolute stereochemistry.

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
methyl-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 159634-47-6
CMF C27 H36 N4 O5 S

Absolute stereochemistry.



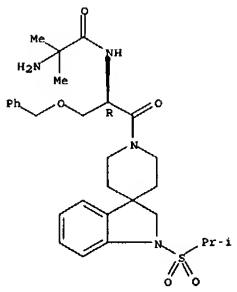
CM 2

CRN 75-75-2
CMF C H4 O3 S

RN 180465-75-2 CAPLUS
CN Propanamide,
2-amino-N-[2-[5-fluoro-1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 180466-14-2 CAPLUS
CN Acetic acid, [[1'-[N-(2-methylalanyl)-O-(phenylmethyl)-D-seryl]spiro[3H-indole-3,4'-piperidin]-1(2H)-yl]sulfonyl]-, 6-[[5-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-1-oxopentyl]amino]hexyl ester, [3aS-(3aα,4β,6aα)]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

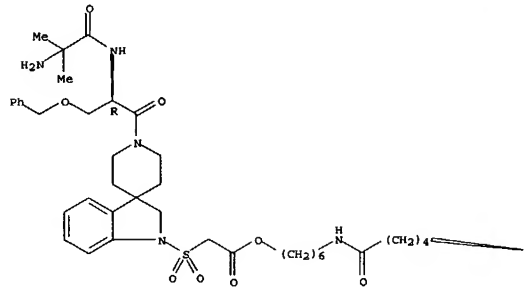
CM 1

CRN 180466-13-1
CMF C44 H63 N7 O9 S2

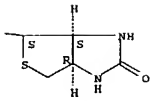
Absolute stereochemistry.

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

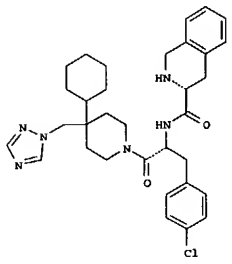
CM 2

CRN 76-05-1
CMF C2 H F3 O2

5/13/2004

=> d abs bib fhitstr 1-6

L5 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
GI

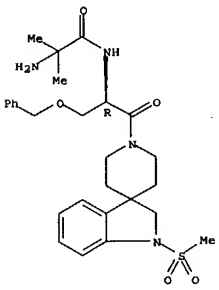


I

AB Synthetic and natural peptides that act as nonselective melanocortin receptor agonists have been found to be anorexigenic and to stimulate erectile activity. We report the design and development of (I), a potent, selective (1184-fold vs. MC3R, 350-fold vs. MC5R), small-mol. agonist of the MC4 receptor. Pharmacol. testing confirms the food intake lowering effects of MC4R agonism and suggests another role for the receptor in the stimulation of erectile activity.
AN 2002:699493 CAPLUS
DN 137:362928
TI Design and pharmacology of N-[(3R)-1,2,3,4-tetrahydroisoquinolinium-3-ylcarbonyl]-(1R)-1-(4-chlorobenzyl)-2-[4-cyclohexyl-4-(1H-1,2,4-triazol-1-ylmethyl)piperidin-1-yl]-2-oxoethylamine (1), a potent, selective, melanocortin subtype-4 receptor agonist
AU Sebhat, Iyassu K.; Martin, William J.; Ye, Zhixiong; Barakat, Khaled; Mosley, Ralph T.; Johnston, David B. R.; Bakshi, Raman; Palucki, Brenda; Weinberg, David H.; MacNeil, Tanya; Kalyani, Rubana N.; Tang, Rui; Stearns, Ralph A.; Miller, Randy R.; Tamvakopoulos, Constantin; Strack, Alison M.; McGowan, Erin; Cashen, Doreen E.; Drisko, Jennifer E.; Hom, Gary J.; Howard, Andrew D.; MacIntyre, D. Euan; van der Ploeg, Lex H. T.; Patchett, Arthur A.; Nargund, Ravi P.
CS Departments of Chemistry, Pharmacology, Obesity Research, and Drug Metabolism, Merck Co. Inc., Rahway, NJ, 07065-0900, USA
SO Journal of Medicinal Chemistry (2002), 45(21), 4589-4593
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English

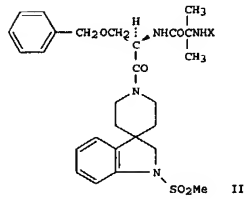
L5 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
IT **159634-47-6**
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(design and pharmacol. of melanocortin 4 receptor agonist)
RN 159634-47-6 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
GI



II

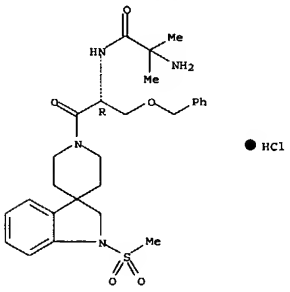
AB This invention is concerned with polymorphic forms of the compound N-[1(R)-[(1,2-dihydro-1-methanesulfonylspiro[3H-indole-3,4'-piperdin]-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide methanesulfonate (I). I is a growth hormone secretagogue that is useful in food animals to promote their growth thereby rendering the production of edible meat products more efficient, and in humans, to treat physiol. or medical conditions. The present invention is also concerned with the formulations in the treatment of certain disorders. Thus, compound (II; X = BOC) (preparation given) was treated with MeSO3H to give the title compound II.MeSO3H (X = H).
AN 1998:414732 CAPLUS
DN 129:67698
TI Polymorphic forms of a growth hormone secretagogue
IN Draper, Jerome P.; Kaufman, Michael J.; Dubost, David C.; McCauley, James A.; Vandrilla, Jennifer L.; Varsolona, Richard J.
PA Merck and Co., Inc., USA
SO U.S., 25 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5767124	A	19980616	US 1996-736170	19961023
CN 1205703	A	19990120	CN 1996-199328	19961023
CN 1067687	B	20010627		
PRAI US 1996-736170	A	19961023		

OS CASREACT 129:67698
IT **159633-92-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminomethylpropanamide derivs. for the treatment of physiol. or medical conditions and certain disorders)
RN 159633-92-8 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-

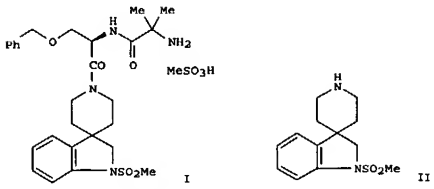
L5 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
GI



I

II

AB A novel convergent process for the preparation of the compound N-[1(R)-[(1,2-dihydro-1-methanesulfonyl-spiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide methanesulfonamide (I) is claimed. The above compound I is synthesized from the reactants (R)-PhCH2OCH2CH(NH2)CO2Me, BocNHC(Me2)CO2H and spiro compound II (which is synthesized in several steps from isonipecotic acid, PhNHNH2 and MeSO2Cl) with an overall yield of 56% and 99.9% purity. This compound may be used to treat conditions which require the stimulation of growth hormone production, or secretion such as in humans with a deficiency of natural growth hormone, or in animals used for food or wool production where the stimulation of growth hormone will result in a larger, more productive animal.

AN 1998:293521 CAPLUS
DN 128:321949
TI Preparation of N-[1(R)-[(1,2-dihydro-1-methanesulfonyl-spiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide methanesulfonamide, a growth hormone secretagogue
IN Dorziotis, Ilias; Houpis, Ioannis; Molina, Audrey; Volante, Ralph
PA Merck & Co., Inc., USA; Dorziotis, Ilias; Houpis, Ioannis; Molina, Audrey; Volante, Ralph
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9818815	A1	19980507	WO 1997-US19063	19971021

W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN,

L5 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

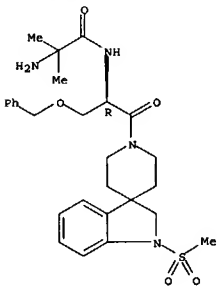
AU 9749934	A1	19980522	AU 1997-49934	19971021
US 6046333	A	20000404	US 1997-955124	19971021
PRAI US 1996-29454P	P	19961025		
GB 1996-25815	A	19961212		
WO 1997-US19063	W	19971021		

IT 159752-10-0P
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation of spiroindolepiperidinyl derivative of aminoisobutyrylserinamide as a growth hormone secretagogue)
RN 159752-10-0 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 159634-47-6
CMF C27 H36 N4 O5 S

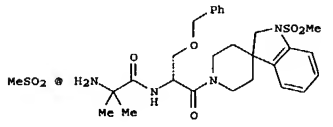
Absolute stereochemistry.



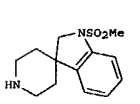
CM 2

CRN 75-75-2
CMF C H4 O3 S

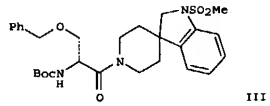
L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
GI



I



II



III

AB The present invention is directed to a novel process for the preparation of N-[1(R)-[(1,2-dihydro-1-methanesulfonylspiro[3H-indole-3,4'-piperdin]-1'-yl)carbonyl]-2-(benzyloxy)ethyl]-2-amino-2-methylpropanamide methanesulfonate (I) and which has the ability to stimulate the release of natural or endogenous growth hormone. I may be used to treat conditions which require the stimulation of growth hormone production or secretion such as in humans with a deficiency of natural growth hormone or in animals used for food or wool production where the stimulation of growth hormone will result in a larger, more productive animal. Thus, peptide coupling of spiropiperidine II (preparation given) with Boc-D-Ser(CH2Ph)-OH (Boc = Me3CO2C) in the presence of DCC and HOBt in aqueous iso-Pr acetate gave 93% adduct III, which was deprotected with MeSO3H in MeOH or EtOH, further coupled with Boc-Aib-OH (Aib = α-aminoisobutyric acid) using DCC and HOBt in aqueous iso-Pr acetate, deprotected with MeSO3H in EtOH, and converted into salt I with MeSO3H in EtOAc.

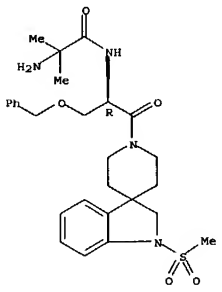
AN 1998:165466 CAPLUS
DN 128:205149
TI Process for the preparation of a growth hormone secretagogue
IN Houghton, Peter G.; Molina, Audrey; Houpis, Joannis; Lynch, Joseph E.; Volante, Ralph P.
PA Merck and Co., Inc., USA
SO U.S., 24 pp.
CODEN: USXXAM
DT Patent
LA English

L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5723616	A	19980303	US 1996-736173	19961023
PRAI US 1996-736173		19961023		

OS CASREACT 128:205149
IT **159634-47-6DP**, N-protected derivs.
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of growth hormone secretagogue using DCC in aqueous iso-Pr acetate)
RN 159634-47-6 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



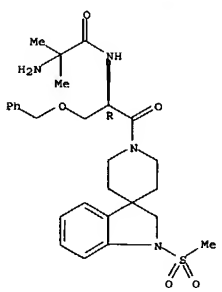
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
AB A review with 183 refs. Growth hormone-releasing peptides (GHRPs) are synthetic, non-natural peptides endowed with potent stimulatory effects on somatotrope secretion in animals and humans. They have no structural homol. with GHRH and act via specific receptors present either at the pituitary or the hypothalamic level both in animals and in humans. The GHRP receptor has been cloned and, interestingly, it does not show sequence homol. with other G-protein-coupled receptors known so far. This evidence strongly suggests the existence of a natural GHRP-like ligand which, however, has not yet been found. The mechanisms underlying the GHRP effect are still unclear. At present, several data favor the hypothesis that GHRPs could act by counteracting somatostatinergic activity both at the pituitary and the hypothalamic level and/or, at least partially, via a GHRH-mediated mechanism. However, the possibility that GHRPs act via an unknown hypothalamic factor (U factor) is still open. GHRP-6 was the first hexapeptide to be extensively studied in humans. More recently, a heptapeptide, GHRP-1, and two other hexapeptides, GHRP-2 and Hexarelin, have been synthesized and are now available for human studies. Moreover, non-peptidyl GHRP mimetics have been developed which act via GHRP receptors and their effects have been clearly demonstrated in animals and in humans in vivo. Among non-peptidyl GHRPs, MK-0677 seems the most interesting mol. The GH-releasing activity of GHRPs is marked and dose-related after i.v., s.c., intranasal and even oral administration. The effect of GHRPs is reproducible and undergoes partial desensitization, more during continuous infusion, less during intermittent administration: in fact, prolonged administration of GHRPs increases IGF-I levels both in animals and in humans. The GH-releasing effect of GHRPs does not depend on sex but undergoes age-related variations. It increases from birth to puberty, persists at a similar level in adulthood and decreases thereafter. By the sixth decade of life, the activity of GHRPs is reduced but it is still marked and higher than that of GHRH. The GH-releasing activity of GHRPs is synergistic with that of GHRH, is not affected by opioid receptor antagonists, such as naloxone, and is only blunted by inhibitory influences, including neurotransmitters, glucose, free fatty acids, glucocorticoids, recombinant human GH and even exogenous somatostatin, which are known to almost abolish the effect of GHRH. GHRPs maintain their GH-releasing effect in somatotrope hypersecretory states such as in acromegaly, **anorexia** nervosa and hyperthyroidism. Their good GH-releasing activity has been shown in some but not in other somatotrope hyposecretory states. In fact, reduced GH responses after GHRP administration have been reported in idiopathic GH deficiency as well as in idiopathic short stature, in obesity and in hypothyroidism, while in patients with pituitary stalk disconnection or Cushing's syndrome the somatotrope responsiveness to GHRPs is almost absent. In short children an increase in height velocity has also been reported during chronic GHRP treatment. Thus, based on their marked GH-releasing effect even after oral administration, GHRPs offer their own clin. usefulness for treatment of some GH hyposecretory states.
AN 1997:375774 CAPLUS
DN 127:90522
TI Growth hormone-releasing peptides
AU Ghigo, E.; Arvat, E.; Muccioli, G.; Camanni, F.
CS Division of Endocrinology, Dep. of Internal Medicine and Division of Pharmacology, Dep. of Anatomy, Pharmacology and Forensic Medicine, University of Turin, Italy
SO European Journal of Endocrinology (1997), 136(5), 445-460
CODEN: EJOEEP; ISSN: 0804-4643
PB BioScientifica
DT Journal; General Review
LA English
IT **159752-10-0**, MK 677
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(growth hormone-releasing peptides)
RN 159752-10-0 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 159634-47-6
CMF C27 H36 N4 O5 S

Absolute stereochemistry.



CM 2

CRN 75-75-2

L5 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CMF C H4 O3 S

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

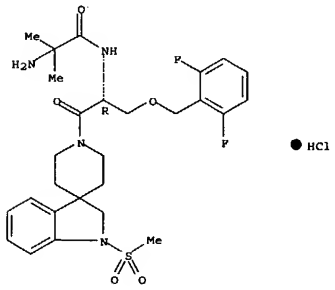
AB There are disclosed certain novel compds. identified as spiro piperidines and homologs I and II wherein: R1 = e.g., C1-10 alkyl, aryl, aryl-(C1-6 alkyl); R2 = e.g., H, C1-6 alkyl, C3-7 cycloalkyl; R3a and R3b are independently, e.g., H, halo, C1-6 alkyl; R4 and R5 are independently, H, C1-6 alkyl, substituted C1-6 alkyl where the substituents on alkyl are, e.g., 1 to 5 halo, 1 to 3 hydroxy; R6 is H or C1-6 alkyl; A is (CH2)xCR7R7a(CH2)y or Z(CH2)xCR7R7a(CH2)y wherein x and y are independently 0, 1, 2, or 3; Z is NR2 or O; R7 and R7a are independently, e.g., H, C1-6 alkyl, OR2; B, D, E, and F are independently selected from CR8R10, O, CO, SOm, NR9, wherein one or two of B, D, E, or F may be optionally absent to provide a 5, 6, or 7-membered ring; R8 and R10 are independently, e.g., H, R2, OR2; R9 = e.g., R2, COR2, SO2R2; m is 0, 1, or 2; n is 1 or 2; G, H, I and J are carbon, nitrogen, sulfur or oxygen atoms, such that one or two is a heteroatom, and where one of G, H, I or J may be optionally absent to afford a 5 or 6 membered heterocyclic aromatic ring; and the pharmaceutically acceptable salts and individual diastereomers thereof, which promote the release of growth hormone in humans and animals (no data). This property can be utilized to promote the growth of food animals to render the production of edible meat products more efficient, and in humans, to treat physiol. or medical conditions characterized by a deficiency in growth hormone secretion, such as short stature in growth hormone deficient children, and to treat medical conditions which are improved by the anabolic effects of growth hormone. Growth hormone releasing compns. containing such spiro compds. as the active ingredient thereof are also disclosed. Thus, e.g., 1'-(t-butyloxycarbonyl)spiro[1H-indene-1,4'-piperidine] was subjected to hydroboration/oxidation, to provide 1'-(t-butyloxycarbonyl)-2,3-dihydro-3-oxospiro[1H-indene-1,4'-piperidine]; deprotection followed by trifluoroacetylation afforded the trifluoroacetamide; Schmidt reaction of the latter provided 3,4-dihydro-2-oxospiro[piperidine-4,4'(1H)-quinoline] trifluoroacetamide (together with its spiroisoquinoline isomer); saponification followed by coupling with α(R)-[[2-[[(1,1-dimethylethoxy)carbonyl]amino]-2,2-dimethyl-1-oxoethyl]amino]-1H-indole-3-propanoic acid (preparation given) and deprotection provided N-[1(R)-[(3,4-dihydro-2-oxospiro[piperidine-4,4'(1H)-quinolin]-1'-yl)carbonyl]-2-(indol-3-yl)ethyl]-2-amino-2-methylpropanamide hydrochloride (III.HCl).
AN 1996:469925 CAPLUS
DN 125:196372
TI Spiro piperidines which promote release of growth hormone

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
IN Chen, Meng-Hsin; Johnston, David B. R.; Nargund, Ravi P.; Patchett, Arthur A.; Tata, James R.; Yang, Lihu
PA Merck and Co., Inc., USA
SO U.S., 48 pp., Cont.-in-part of U.S. Ser. No. 989,322, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5536716	A	19960716	US 1993-147226	19931103
	WO 9413696	A1	19940623	WO 1993-US11038	19931115
	W: BB, BG, BR, BY, CZ, FI, HU, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ				
	RW: BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	WO 9419367	A1	19940901	WO 1993-US11137	19931115
	W: BB, BG, BR, BY, CZ, FI, HU, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ				
	RW: BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	HU 72076	A2	19960328	HU 1995-1683	19931115
	HU 73228	A2	19960729	HU 1995-1681	19931115
	PL 176993	B1	19990831	PL 1993-309331	19931115
	RU 2168512	C2	20010610	RU 1995-113349	19931115
	SK 282166	B6	20011106	SK 1995-759	19931115
	CA 2110670	AA	19940612	CA 1993-2110670	19931203
	CA 2110670	C	20010417		
	CA 2110672	AA	19940612	CA 1993-2110672	19931203
	EP 615977	A1	19940921	EP 1993-309867	19931208
	EP 615977	B1	20020703		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	AT 220071	E	20020715	AT 1993-309867	19931208
	PT 615977	T	20021031	PT 1993-309867	19931208
	ES 2177538	T3	20021216	ES 1993-309867	19931208
	AU 9352320	A1	19940623	AU 1993-52320	19931210
	AU 673552	B2	19961114		
	AU 9352321	A1	19940623	AU 1993-52321	19931210
	AU 673017	B2	19961024		
	ZA 9309272	A	19940808	ZA 1993-9272	19931210
	ZA 9309274	A	19940808	ZA 1993-9274	19931210
	JP 06263737	A2	19940920	JP 1993-341522	19931210
	JP 2509530	B2	19960619		
	HR 931486	B1	20030831	HR 1993-931486	19931210
	CN 1092071	A	19940914	CN 1993-112858	19931211
	CN 1034733	B	19970430		
	FI 9502862	A	19950609	FI 1995-2862	19950609
	FI 9502863	A	19950609	FI 1995-2863	19950609
	NO 9502294	A	19950810	NO 1995-2294	19950609
	NO 9502295	A	19950810	NO 1995-2295	19950609
	US 5652235	A	19970729	US 1996-641311	19960430
PRAI	US 1992-989322	B2	19921211		
	US 1993-146848		19931103		
	US 1993-147226	A	19931103		
	WO 1993-US11038	W	19931115		
	WO 1993-US11137	W	19931115		

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
OS MARPAT 125:196372
IT **159633-90-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(spiro piperidines which promote release of growth hormone)
RN 159633-90-6 CAPLUS
CN Propanamide, 2-amino-N-[1-[[(2,6-difluorophenyl)methoxy]methyl]-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxoethyl]-2-methyl-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

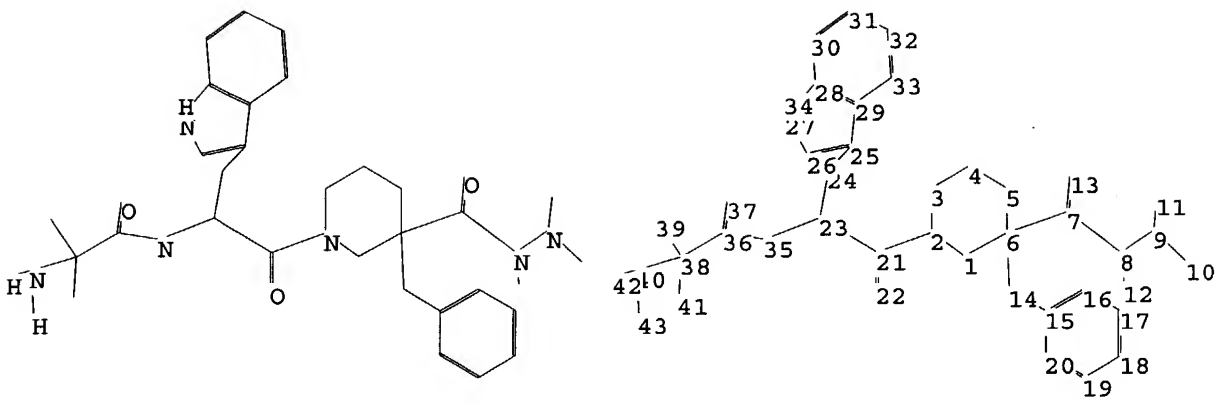
Absolute stereochemistry.



5/13/2004

```
 NEWS 18  May 12  EXTEND option available in structure searching
 NEWS 19  May 12  Polymer links for the POLYLINK command completed in REGISTRY
 NEWS 20  May 17  FRFULL now available on STN

 NEWS EXPRESS  MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:44:29 ON 19 MAY 2004

=> file registry
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     2.10       2.10

FILE 'REGISTRY' ENTERED AT 15:50:12 ON 19 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   18 MAY 2004  HIGHEST RN 683203-75-0
DICTIONARY FILE UPDATES:  18 MAY 2004  HIGHEST RN 683203-75-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Stnexp4 corrupted\QUERIES\10649386-2.str
```

5/13/2004



chain nodes :
7 8 9 10 11 12 13 14 21 22 23 24 34 35 36 37 38 39 40 41 42 43

ring nodes :
1 2 3 4 5 6 15 16 17 18 19 20 25 26 27 28 29 30 31 32 33
chain bonds :
2-21 6-7 6-14 7-8 7-13 8-9 8-12 9-10 9-11 14-15 21-22 21-23 23-24
23-35 24-25 27-34 35-36 36-37 36-38 38-39 38-40 38-41 40-42 40-43
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20 25-26
25-29 26-27 27-28 28-29 28-30 29-33 30-31 31-32 32-33
exact/norm bonds :
1-2 1-6 2-3 2-21 3-4 4-5 5-6 7-8 7-13 8-9 8-12 9-10 9-11 21-22 23-35
25-26 25-29 26-27 27-28 35-36 36-37 38-40
exact bonds :
6-7 6-14 14-15 21-23 23-24 24-25 27-34 36-38 38-39 38-41 40-42 40-43
normalized bonds :
15-16 15-20 16-17 17-18 18-19 19-20 28-29 28-30 29-33 30-31 31-32 32-33

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:Atom 16:Atom 17:Atom 18:Atom
19:Atom 20:Atom 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:Atom 26:Atom 27:Atom
28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 33:Atom 34:CLASS 35:CLASS 36:CLASS
37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS 43:CLASS

L1 STRUCTURE UPLOADED

=> d l1

5/13/2004

L1 HAS NO ANSWERS
L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 15:50:33 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 2 TO ITERATE

100.0% PROCESSED 2 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 2 TO 124
PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

=> s l1 ful
FULL SEARCH INITIATED 15:50:37 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 33 TO ITERATE

100.0% PROCESSED 33 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.01

L3 5 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 155.42 157.52

FILE 'CAPLUS' ENTERED AT 15:50:42 ON 19 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 19 May 2004 VOL 140 ISS 21
FILE LAST UPDATED: 18 May 2004 (20040518/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

5/13/2004

```
=> s l3
L4            3 L3

=> s l4 and (food or anorexia or diabetes or weight)
         291349 FOOD
          66103 FOODS
         310265 FOOD
                   (FOOD OR FOODS)
           5286 ANOREXIA
              7 ANOREXIAS
           5286 ANOREXIA
                   (ANOREXIA OR ANOREXIAS)
          88894 DIABETES
          99841 WEIGHT
          12585 WEIGHTS
         108143 WEIGHT
                   (WEIGHT OR WEIGHTS)
        1355317 WT
         100236 WTS
        1406446 WT
                   (WT OR WTS)
        1436145 WEIGHT
                   (WEIGHT OR WT)
L5            1 L4 AND (FOOD OR ANOREXIA OR DIABETES OR WEIGHT)

=> d abs bib hitstr
```

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN

AB Compds. that are ligands for the receptor GHS-R 1A, as well as pharmaceutically acceptable salts thereof, are useful for the manufacture of medicaments for the regulation of **food** intake.

AN 2001:581723 CAPLUS
DN 135:147451
TI Use of compounds for the regulation of **food** intake
IN Andersen, Maibritt Bansholm; Hansen, Birgit Sehested; Raun, Kirsten; Tullin, Soren; Thim, Lars
PA Novo Nordisk A/S, Den.
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

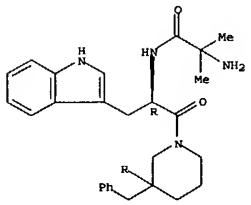
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001056592	A1	20010809	WO 2001-DK64	20010129
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001020012	A1	20010906	US 2001-771770	20010129
US 2004063636	A1	20040401	US 2003-649386	20030827
PRAI DK 2000-161	A	20000201		
DK 2000-1107	A	20000717		
US 2000-181303P	P	20000209		
US 2001-771770	B1	20010129		

IT **353289-95-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(use of compds. for regulation of **food** intake that are ligands of growth hormone secretagogue type 1A receptors (GHS-R 1A) in relation to growth hormone release)
RN 353289-95-9 CAPLUS
CN 3-Piperidinecarboxylic acid, 1-(2-methylalanyl-D-tryptophyl)-3-(phenylmethyl)-, trimethylhydrazide (9CI) (CA INDEX NAME)

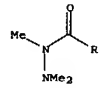
Absolute stereochemistry.
Currently available stereo shown.

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

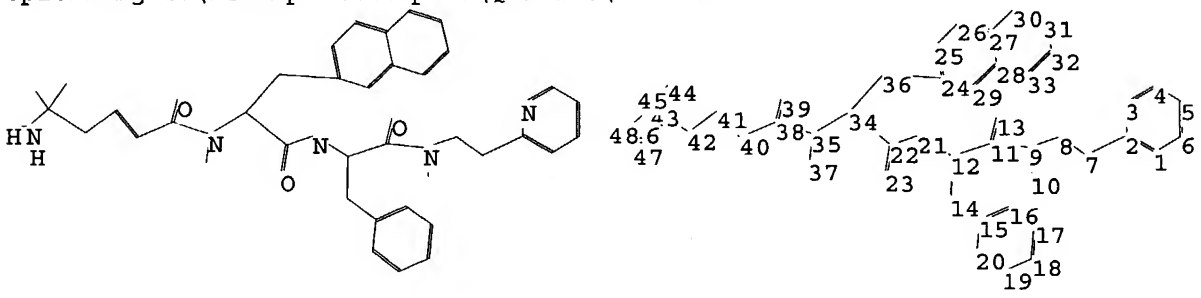
5/13/2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Stnexp4 corrupted\QUERIES\10649386-3.str



chain nodes :
7 8 9 10 11 12 13 14 21 22 23 34 35 36 37 38 39 40 41 42 43 44
45 46 47 48
ring nodes :
1 2 3 4 5 6 15 16 17 18 19 20 24 25 26 27 28 29 30 31 32 33
chain bonds :
2-7 7-8 8-9 9-10 9-11 11-12 11-13 12-14 12-21 14-15 21-22 22-23 22-34
24-36 34-35 34-36 35-37 35-38 38-39 38-40 40-41 41-42 42-43 43-44 43-45
43-46 46-47 46-48
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20 24-29
24-25 25-26 26-27 27-28 27-30 28-29 28-33 30-31 31-32 32-33
exact/norm bonds :
8-9 9-10 9-11 11-13 12-21 21-22 22-23 34-35 35-37 35-38 38-39 43-46
exact bonds :
2-7 7-8 11-12 12-14 14-15 22-34 24-36 34-36 38-40 40-41 41-42 42-43
43-44 43-45 46-47 46-48
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20 24-29
24-25 25-26 26-27 27-28 27-30 28-29 28-33 30-31 31-32 32-33

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:Atom 16:Atom 17:Atom 18:Atom
19:Atom 20:Atom 21:CLASS 22:CLASS 23:CLASS 24:Atom 25:Atom 26:Atom 27:Atom
28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 33:Atom 34:CLASS 35:CLASS 36:CLASS
37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS 43:CLASS 44:CLASS
45:CLASS 46:CLASS 47:CLASS 48:CLASS

10649386

```
L6      STRUCTURE UPLOADED

=> d l6
L6 HAS NO ANSWERS
L6              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l6
SAMPLE SEARCH INITIATED 16:18:34 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      0 TO ITERATE

100.0% PROCESSED       0 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE   **COMPLETE**
                        BATCH    **COMPLETE**
PROJECTED ITERATIONS:            0 TO         0
PROJECTED ANSWERS:               0 TO         0

L7            0 SEA SSS SAM L6

=> s l6 ful
FULL SEARCH INITIATED 16:18:39 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     29 TO ITERATE

100.0% PROCESSED      29 ITERATIONS                               2 ANSWERS
SEARCH TIME: 00.00.01

L8            2 SEA SSS FUL L6

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     155.42     328.48

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                       0.00      -0.69

FILE 'CAPLUS' ENTERED AT 16:18:45 ON 19 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
```

5/13/2004

FILE COVERS 1907 - 19 May 2004 VOL 140 ISS 21
FILE LAST UPDATED: 18 May 2004 (20040518/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s l8
L9 2 L8

=> d abs bib hitstr 1-2

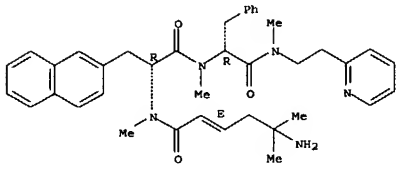
L9 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
AB Compds. that are ligands for the receptor GHS-R 1A, as well as pharmaceutically acceptable salts thereof, are useful for the manufacture of medicaments for the regulation of food intake.
AN 2001:581723 CAPLUS
DN 135:147451
TI Use of compounds for the regulation of food intake
IN Andersen, Maibritt Bansholm; Hansen, Birgit Sehested; Raun, Kirsten; Tullin, Soren; Thim, Lars
PA Novo Nordisk A/S, Den.
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001056592	A1	20010809	WO 2001-DK64	20010129
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001020012	A1	20010906	US 2001-771770	20010129
US 2004063636	A1	20040401	US 2003-649386	20030827
PRAI DK 2000-161	A	20000201		
DK 2000-1107	A	20000717		
US 2000-181303P	P	20000209		
US 2001-771770	B1	20010129		

IT **267225-30-9**, NNC 26-1187
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(use of compds. for regulation of food intake that are ligands of growth hormone secretagogue type 1A receptors (GHS-R 1A) in relation to growth hormone release)
RN 267225-30-9 CAPLUS
CN D-Phenylalaninamide, N-[(2E)-5-amino-5-methyl-1-oxo-2-hexenyl]-N-methyl-3-(2-naphthalenyl)-D-alanyl-N,Nα-dimethyl-N-[2-(2-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)

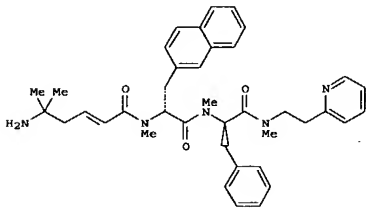
Absolute stereochemistry.
Double bond geometry as shown.

L9 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
GI



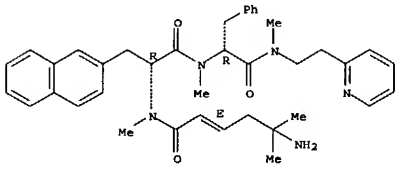
I

AB The invention relates to novel compds., compns. containing them, and their use for treating medical disorders resulting from a deficiency in growth hormone. Preparation of e.g. I is described.
AN 2000:314733 CAPLUS
DN 132:318046
TI Compounds with growth hormone-releasing properties
IN Ankersen, Michael; Richter, Lutz Stefan
PA Novo Nordisk A/S, Den.
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000026252	A1	20000511	WO 1999-DK594	19991103
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6566337	B1	20030520	US 1999-431864	19991102
BR 9915009	A	20010807	BR 1999-15009	19991103
EP 1127071	A1	20010829	EP 1999-955835	19991103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002528556	T2	20020903	JP 2000-579638	19991103
ZA 2001002997	A	20011119	ZA 2001-2997	20010411
NO 2001002169	A	20010502	NO 2001-2169	20010502
PRAI DK 1998-1414	A	19981103		
US 1998-107663P	P	19981109		

L9 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
WO 1999-DK594 W 19991103
OS MARPAT 132:318046
IT **267225-30-9P 267225-40-1P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(compds. with growth hormone-releasing properties)
RN 267225-30-9 CAPLUS
CN D-Phenylalaninamide, N-[(2E)-5-amino-5-methyl-1-oxo-2-hexenyl]-N-methyl-3-(2-naphthalenyl)-D-alanyl-N,Nα-dimethyl-N-[2-(2-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

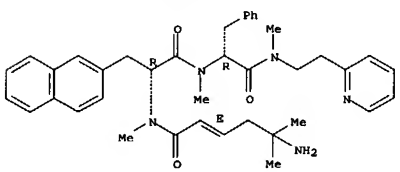


RN 267225-40-1 CAPLUS
CN D-Phenylalaninamide, N-[(2E)-5-amino-5-methyl-1-oxo-2-hexenyl]-N-methyl-3-(2-naphthalenyl)-D-alanyl-N,Nα-dimethyl-N-[2-(2-pyridinyl)ethyl]-, monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 267225-30-9
CMF C39 H47 N5 O3

Absolute stereochemistry.
Double bond geometry as shown.



L9 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

CM 2

CRN 64-19-7
CMF C2 H4 O2

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT